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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/674,092	02/27/2001	Marcus Keep	30-200P	1549

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EXAMINER
MOHAMED, ABDEL A

ART UNIT	PAPER NUMBER
1653	12

DATE MAILED: 03/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/674,092	KEEP ET AL.	
	Examiner	Art Unit	
	Abdel A. Mohamed	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7,10* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

ACKNOWLEDGMENT OF PRIORITY, IDS, SEQUENCE LISTING, AMENDMENT, STATUS OF THE APPLICATION AND CLAIMS

1. This application is filed under 35 U.S.C. 371 on 2/27/01 having a filing date of 2/26/99 of PCT/US99/04359. Receipt is acknowledged of papers submitted under 35 U.S.C. § 119, which papers have been placed of record in the file. Also, the preliminary amendment filed 2/27/01 and the information disclosure statement (IDS) and Form PTO-1449 filed 10/26/00 and 10/24/02, respectively are acknowledged, entered and considered. In view of Applicant's request claim 7 has been amended. Thus, claims 1-8 are now pending in the application.

ABSTRACT MISSING

2. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

CLAIMS REJECTION-35 U.S.C. § 112^{2nd} PARAGRAPH

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite in the recitation "compromizing" and claims 3-6 are indefinite in the recitation "compromises" The claims have been read as if they say "comprising" and "comprises", respectively. It is believed to be typographical error. Appropriate correction is required.

Claims 1, 3-6 and 8 are indefinite in the recitation the acronym "DMSO". Use of full terminology at least in the first occurrence would obviate this rejection.

In claim 8, the phrase "such as" render the claim indefinite because use of a narrower range within a broader range in the same claim makes the claim indefinite since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. One could not tell from such a claim if the narrower range or limitation is a restriction or limitation on the broader range or limitation. See "selected from the group consisting of" instead.

CLAIM REJECTION-35 U.S.C. § 102(b)

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2 are rejected under 35 U.S.C. 102(b) as being anticipated by Lebel et al., (Int. Arch. Allergy. Immunol., Vol. 116, pp. 284-287, 1998).

Lebel et al., disclose a composition comprising a cyclosporin dissolved in dimethyl sulfoxide (DMSO) wherein the cyclosporin is cyclosporin A. To the extent that cyclosporin dissolved in DMSO is in a physiological buffer it is considered to be a pharmaceutical composition (See e.g., pages 284 and 286) and anticipates claims 1 and 2.

5. Claims 1-2 are rejected under 35 U.S.C. 102(b) as being anticipated by Kessler et al., (Biochemical Pharmacology, Vol. 40, No. 1, pp. 169-173, 1990).

Kessler et al., disclose a composition comprising a cyclosporin dissolved in polar solvent DMSO wherein the cyclosporin is cyclosporin A. To the extent that cyclosporin dissolved in DMSO is in a physiological buffer it is considered to be a pharmaceutical composition (See e.g., pages 172-172) and anticipates claims 1 and 2.

CLAIMS REJECTION-35 U.S.C. § 103(a)

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 3-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lebel et al., (Int. Arch. Allergy. Immunol., Vol. 116, pp. 284-287, 1998) taken with Falk et al., (U.S. Patent No. 5,827,834).

Lebel et al., disclose a composition comprising a cyclosporin dissolved in dimethyl sulfoxide (DMSO) wherein the cyclosporin is cyclosporin A. To the extent that cyclosporin dissolved in DMSO is in a physiological buffer it is considered to be a pharmaceutical composition (See e.g., pages 284 and 286). The reference of Lebel et al., differs from claims 3-8 in failing to teach methods for administering said cyclosporin and DMSO solution by injection into the cerebrospinal fluid, intra-ocular, intravestibular, into adjacent to the brain, or spinal cord, or intravenous, intraarterial, intraparenchymal spaces or orally, rectally, nasally or dermally to a patient wherein the cyclosporin is cyclosporin A, or functional derivatives, metabolites, variants or salts thereof, and an article of manufacture comprising packaging material and pharmaceutical agent wherein said pharmaceutical agent comprises DMSO and cyclosporin formulation thereof.

The prior art of Falk et al., (U.S. Patent No. 5,827,834) clearly teaches the method of administering a medicinal agent in general which includes immunosuppressant such as cyclosporins in treating a disease or condition in mammals (See e.g., col. 10, lines 3 to 28). The medical agent comprises methyl sulfoxide (DMSO) as a carrier transport-type molecule in an injectable formulation. Thus, combinations and formulations (for example an injectable formulation) are provided for administration to a mammal for the treatment of a disease or condition (See e.g., col. 10, lines 3 to 6), which combinations or formulations employ or incorporate as the case may be a therapeutically effective non-toxic amount of a medicinal and/or therapeutic agent to treat disease or condition for example a free radical scavenger or anti-cancer agent or anti-viral agent, or anti-bacterial agent, or analgesic or immunosuppressants (for example cyclosporins) etc. (See e.g., col. 10, lines 6-28), sufficient to facilitate the agent's penetration through the tissue (including scar tissue), at the site to be treated through the cell membranes into the individual cell to be treated (See e.g., col. 10, lines 34-37). When such combinations and formulations are administered to patients suffering from disease or condition, the disease or condition is improved. Further, the formulation can be administered among other methods, intravenously, intra arterially, intraperitoneally, intrapleurally, transdermally, on the skin (topically), rectally, orally or by direct injection (for example into a tumor, into an abscess or similar disease focus i.e., this statement may encompass cerebro spinal fluid space or adjacent to the brain or spinal cord) (See e.g., col. 10, lines 41-44). Also, the patent shows the administration of pharmaceutical agent in combination with DMSO in patients suffering from

brain tumors resulted in reduction of swelling in acute brain and spinal edema. Thus, clearly showing the use of DMSO as a carrier/penetrating agent in a medicinal formulation wherein the medicinal agent or formulation could be the combination of DMSO and any agent of interest which may include cyclosporins (See e.g., abstract, cols. 3-4, cols. 10-12, col. 17, Cases I, III and IX of '834 patent) as directed to claims 3-6. Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have combined the teachings of Lebel et al., with Falk et. al. patent in order to administer cyclosporin and DMSO by any one of the mode of administration recited in claims 3-6. The artisan of ordinary skill in the art utilizing the methods of Falk et. al., patent (i.e., the secondary reference) would have obtained the improvement when such combinations and formulations (as disclosed in the primary reference) are administered to patients suffering from the disease or condition.

With respect to claim 7, the method requires administering cyclosporin A, or functional derivatives, metabolites, variants or salts thereof. Given the teachings of the secondary reference of Falk et al., one of ordinary skill in the art would be able to adapt the above scheme of applying a specific cyclosporin such as functional derivatives of cyclosporin, metabolites of cyclosporin, variants of cyclosporin or salts thereof because the secondary reference disclose cyclosporins in general without specifying particular ones as disclosed in the primary reference (i.e., cyclosporin A). Further, such features (i.e., using cyclosporins in general) are known or suggested in the art, as seen in the secondary reference, and including such features into the composition (only cyclosporin A) of the primary reference of Lebel et al., (See e.g., abstract) would have been

obvious to one of ordinary skill in the art to obtain the known and recognized functions and advantages thereof.

With respect to claim 8, an article of manufacture comprising packaging material and pharmaceutical agent or formulation claimed; but, where the above reference differs from claim 8 in not teaching *per se* the formulation claimed in a packaging material. However, it is the Examiner's position that it would have been obvious to package the composition required for the method into packaging material and/or kit format of the well known commercial expediency of dong so. Therefore, in view of the above, in view of the combined teachings of the prior art, and in the absence of evidence to the contrary, modifications such as the selection of an appropriate cyclosporin and formulations of packaging material and/or kit thereof, would have resulted in the claimed invention which was *prima facie* obvious to make and use at the time it was made.

CONCLUSION AND FUTURE CORRESPONDENCE

6. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed whose telephone number is (703) 308-3966. The examiner can normally be reached on Monday through Friday from 7:30 a.m. to 5:00 p.m. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached on (703) 308-2923. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

AAM Mohamed/AAM

March 10, 2003